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EXAMINER	
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THIS APPLICATION IS SUBJECT TO EXAMINATION UNDER THE RULES RELATING TO PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 28 October 19 91 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire three (3) month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-16, 30-33, 37-40, and 71 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-16, 30-33, 37-40, and 71 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office Action.

The amendment to the specification and the claims in the response filed 28 October 1991 is noted. In view of the amendments to the claims, the following grounds of objection and rejection are or remain applicable.

The application remains objected to as indicated in the prior Office Action because of alterations which have not been dated as is required by 37 CFR 1.52(c) and 1.56. A properly executed affidavit or declaration signed by all of the inventors identifying the alterations and stating when the unsigned and/or undated alterations were made is required. If the alterations were made before the signing of the oath or declaration, a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by its Serial Number, filing date and the title is also required. If the alterations were made after the signing of the oath or declarations, a full explanation and cancellation of such alterations is required. Attention is directed to page 8, line 19, page 10, line 24, page 17, lines 30 and 32, page 19, line 23, page 23, line 23, page 24, lines 10 and 24, page 29, lines 13 and 14, page 35, lines 13 and 26, page 39, lines 6 and 8, page 40, line 12, page 41, lines 33 and 34, page 44 (Table 6), which contain initialed but undated corrections to the specification.

The comments in the response (page 3) filed 28 October 1991 asserting that the Examiner has required cancellation is incorrect. Attention is directed to the last line of the prior Office Action at page 2, which indicates "Correction of the foregoing is required.", and that such correction as indicated above and in the prior Office Action indicated in part "A properly executed affidavit or declaration signed by all of the inventors identifying the alterations and stating when the unsigned and/or undated alterations were made is required."

The use of what are apparently trademarks has been noted in this application. It should be capitalized (i.e. the entire word should be

capitalized, not just the first letter). Attention is directed to page 4 of the response filed 28 October 1991.

At least claims 4, 5, 11, 37-40 of this application contain underlining or brackets that are intended to appear in the printed patent or are properly part of the claimed material. The brackets or underlining are not intended to indicate amendments or changes in the claims. Under these conditions, proposed amendments to the claims may not be made by underlining words added or by bracketing words to be deleted. Accordingly, for the purposes of examination, since applicant has indicated in the footnotes of the response that such originally underlined words in the claims are genus names and are properly underlined as originally presented, amended claims have been read in that light. However, as noted above, the manner of amending the claims as is now present in the response is improper. While the claims have been read in the manner indicated by applicant, this does not relieve applicant of the requirement and responsibility to properly amend the claims. The manner in which claims that contain underlining or brackets may be amended is by presentation as a new claim. It is pointed out that double underlining is also an unacceptable manner of amending such claims. See 37 CFR 1.121(d).

Correction is required.

Applicant's election of Group I, claims 1-16, 30-33, 37-40, and new claim 71 in Paper No. 6 is acknowledged. The Office notes that the prior Office Action indicated that the election was made with traverse, however, since applicant did not distinctly and specifically point out the supposed errors in the restriction requirement in the response filed 28 October 1991, the election has been treated as an election without traverse (MPEP 818.03(a)).

35 U.S.C. 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 6, 7, 10, 12, and 13 are rejected under 35 U.S.C. 101 because the invention as is now claimed is directed to non-statutory subject matter and this rejection is necessitated by the amendment to the claims.

The expression vector and microorganism as claimed are found in nature. See the present specification at least at pages 4, 7, and 21 as well as any of McDaniel (BY and AZ), Harper et al. (BX), Wild et al. (AT), and Mulbry et al. (AY), all of which are of record. Note that the terminology vector as is now recited in the claims, unqualified, is any piece of DNA that contains the requisite DNA coding for the enzyme where the naturally occurring bacterial plasmid DNA also contains all of the requisite DNA for effecting expression of the organophosphorous acid anhydrase and when that DNA is in the naturally occurring microorganism, the claims are deemed to be drawn to products of nature as they contain the naturally occurring DNA coding for the organophosphorous acid anhydrase. Absent qualifying language in the claims, the vector and cells possess the biological and functional properties of a naturally occurring DNA, the vector containing that DNA, and the naturally occurring microorganisms containing that naturally occurring vector are found in nature and therefore do not constitute patentable subject matter.

See American Wood v. Fiber Disintegrating Co., 90 U. S. 566 (1974); American Fruit Growers v. Brogdex Co., 283 U. S. 1 (1931); Funk Brothers Seed Co. v. Kalo Inoculant., 33 U. S. 127 (1948); and Diamond v. Chakrabarty, 206 USPQ 193 (1980).

Claim 14 is rejected under 35 U.S.C. 101 because it is directed to non-statutory subject matter. This rejection is necessitated by the amendment to the claim. Note that the claim as is now amended encompasses a cell in an intact human containing the cell(s) and is not statutory subject matter.

The specification remains objected to under 35 U.S.C. 112, first paragraph, as failing to provide a reasonable written description for

practicing the claimed invention for the reasons of record in the prior Office Action.

The comments in the response filed 28 October 1991 have been considered but are not persuasive. The comments apparently indicate that there are differences in the published DNA sequences compared to the sequence in the application for patent, however, given that there are three disparate sequences, it is not clear that one of ordinary skill in the art using solely the disclosure in the application would have obtained that DNA having the sequence of Figure 1. Note in particular the indication in the response at page 15-16 indicating a 2% difference in sequence and the request to alter the sequence of Figure 1 (page 18).

It is not clear what changes have been made in substitute Figure 1, as it is not apparently of record. It is noted that applicants' response cites Ex parte Marsili et al. among others (footnote, page 18-19 of the response), however, in Marsili, the specification was adequately enabling to support the change in formula of a chemical compound (note that a DNA polymer is not the same compound as an imidazole) whereas here, the final product is a specific DNA coding for a specific enzyme where that sequence of bases is a critical feature. Here the specification and the response alone do not show what changes applicants intend to make and whether or not those changes would have been adequately supported by the specification as originally filed, nor has any change been shown to have been an inherent characteristic. Thus, Ex parte Marsili et al. among others is not definitive for showing the precedence of altering the DNA sequence of Figure 1 as originally filed in the instant application. The comments regarding Exhibit A in the response have been considered (page 15+ of the response) and is clearly indicative that the sequence as indicated in the application and those which have been published are disparate. Thus, the query of which sequence is correct still remains and given those disparities, it is apparent that the written description is fatally flawed as the sequence comparison (Exhibit A) shows by indication of several hyphens, "-", defined as a "... base is missing ...", and, that the sequence as originally filed is incomplete as is evident from the comparative

evidence of Exhibit A. Note the numerous hyphens in the sequence indicated to be that which conforms to application figure 1. In the previous Office Action, the specification was objected to because of the apparent disparity between the published sequences and the sequence set forth in the present application. In view of the disparities (Exhibit A filed with the response) and the request to correct the sequence shown in Figure 1, it is now clearly apparent that the present application lacks a reasonable written description for practicing the claimed invention with regard to the correct DNA sequence. Previously, Figure 1 of the present application was in one alternative the correct sequence, however, from Exhibit A, it is now clear that the sequence shown in Figure 1 in the present application is incorrect. Thus, the former objection is not removed by the explanation and exhibit in applicants' present response and that in view of the amended claims and the intention to correct Figure 1, the specification remains objected to.

Claims 1-16, 30-33, 37-40, and 71 are rejected under 35 U.S.C. 112, first paragraph, for the reasons set forth in the objection to the specification in the prior Office Action and as further indicated above. This ground of rejection is now necessitated by the present amendment to the claims. As indicated above, in the previous Office Action, the specification was objected to because of the apparent disparity between the published sequences and that set forth in the present application. The disparities (Exhibit A filed with the response) and the request to correct the sequence shown in Figure 1 now clearly show a lack of a reasonable written description for practicing the claimed invention with regard to the correct DNA sequence. Note that Figure 1 of the present application was in one alternative the correct sequence, however, from Exhibit A, it is now clear that the sequence shown in Figure 1 in the present application is incorrect. Thus, the objection to the specification is not removed by the explanation and exhibit in applicants' present response; and that in view of the amended claims and the intention to correct Figure 1, the objection is not seen as removable by minor correction or explanation of which DNA sequence (the prior art or that of Figure 1 in the present application) is the correct sequence. Thus, the claims as amended are rejected and the rejection is necessitated by the amendments to the claims.

Claims 1-16, 30-33, 37-40, and 71 are rejected under 35 U.S.C. 112, first paragraph, as the disclosure is enabling only for claims limited to a heterologous DNA coding for organophosphorous anhydrase having the sequence of bases shown in Figure 1 and for transformed E. coli and Spodoptera frugiperda Sf9 cells cultured in vitro using the specifically disclosed plasmid constructs. The terminology "DNA sequence" is now indicated in the claims, however, that terminology refers to the abstraction of the DNA polymer onto a piece of paper using the letters "A", "T", "C", and "G" in a particular order and it is simply unclear as to how such an abstraction is the same as the physical entity of the DNA polymer or expression vector as determined by physical, chemical, and biological characteristics. Note the suggestion above with regard to "... DNA having a sequence ..." or for that matter, how such abstraction is used to in the construction of a plasmid and in transforming a host cell. With regard to the terminology "eukaryotic cell", note that without qualification, that reads on a transformed cell in a human and the specification is silent on the matter of constructing a human containing transformed human cells containing the DNA coding for the OPA enzyme. In any event, such claim is also non-statutory subject matter (see the above rejection under 35 U.S.C. 101). This rejection is necessitated by the amendment (response filed 28 October 1991) which broadens the scope of the claims. See MPEP 706.03(n) and 706.03(z).

Claims 1-16, 30-33, 37-40 and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office notes at the outset that all of the pending claims have been amended. Here, claim 1 recites "An ..." and "... comprising a DNA ..." wherein the use of "An" and "a" are suggestive of an alternative DNA whereas in Figure 1 there is only one sequence shown. It is suggested that the "An" and the "a" be replaced with "the". In the alternative, the "An" should be replaced with "The" and "gene comprising a" should be deleted and replaced with "consisitng of a " and the words "having the" inserted after "DNA". In claim 2 (see also the remaining claims) the terminology "DNA sequence" is now

indicated, however, that terminology refers in one interpretation, to the abstraction of the DNA polymer onto a piece of paper using the letters "A", "T", "C", and "G" in a particular order and it is simply unclear as to how such an abstraction is the same as the physical entity of the DNA polymer or expression vector as determined by physical, chemical, and biological characteristics. Note the suggestion above with regard to "... DNA having a sequence ..." or for that matter, how such abstraction is used to in the constuction of a plasmid and in transforming a host cell. Claims 6, 7, 10, 12, 13, as amended are vague and indefinite as to whether or not the claims are drawn to a man-made vector and microorganism containing the plasmid or whether the calims are the naturally occurring plasmids and microorganisms containing same. The terminology vector and microorganism are now unqualified. As such, the claim encompasses any piece of DNA that contains the requisite DNA coding for the enzyme (i.e. the naturally occurring bacterial plasmid DNA where plasmid also occurs in nature in the microorganism and contains all of the requisite DNA for effecting expression of the organophosphorous acid anhydrase). In claim 15 it is not clear what is meant by "derived" as such terminology can mean "obtained from" or "modified so as to be different" whereas "... wherein said cell is an insect cell ..." is clear. In claim 30 it is not clear what portion has been cleaved. does it refer to the first 61 bases, bases 57 to 61, or to only the first "C" of the sequence shown in figure 1? How many bases constitute a "portion"? What defines a "portion"? In this regard, note also claims 31-33 and to claims 37-40 with regard to the 3'-terminus. In claim 71 a promoter and terminator that direct "translation"? Promoters and terminators commonly direct "transcription". Attention is directed to Singleton et al. All of the foregoing is necessitated by the amended claims as the amendment (response filed 28 October 1991) broadens the scope of the claims so as to make them vague and indefinite.

The remarks at pages 19-20 of the response filed 28 October 1991 have been considered but are not convincing as the above ground of rejection is necessitated by amendments to the claims.

Claims 1-3, 5-7, 9, 10, 12-13, 30-32, and 37-39 remain rejected and new claim 71 is rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over McDaniel et al. (BY) for the reasons of record in the prior Office Action.

The comments in the response filed 28 October 1991 have been considered but are not persuasive. It is pointed out that McDaniel, Harper, and Wild are not the same entity as McDaniel, Raushel, and Wild and the relevant portion of the statute indicates "the invention was known or used by others in this country" and McDaniel, Harper, and Wild are the equivalent of "others". It is noted that applicant has cited In re Katz, however, in the Katz decision, 35 U.S.C. 102 (g) was applied where as here, 35 U.S.C. 102 (a) is applied. Note the opinion at page 18 right column, a declaration was filed unlike here where no disclaiming affidavit has been filed and the comments in the response at page 23 regarding Harper and Miller are not in the appropriate declaration format. Applicants have indicated a willingness to also file disclaiming affidavits from both Harper and Miller, however, such affidavits are not of record.

Claims 1-7, 9, 10, 12-13, 30-32, and 37-39 remain rejected and new claim 71 is rejected under 35 U.S.C. 102 (a) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Harper et al. (BX) for the reasons of record in the prior Office Action.

The comments in the response filed 28 October 1991 have been considered but are not persuasive for the reasons set forth above in regard to the McDaniel et al. reference (BY).

Claims 1-7, 9, 10, 12-13, 30-32, and 37-39 remain rejected and new claim 71 is rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over either of Wild et al. (AT) or Mulbry et al. (AY) for the reasons of record in the prior Office Action.

The comments regarding the Wild et al. reference in the response filed 28 October 1991 are noted but not convincing. While the reference indicates that removal of 250 base pairs enhanced activity, note that the reference discloses the DNA coding for the enzyme, vectors containing same and transformed host cells. With regard to the Mulbry et al. reference, note that the reference discloses the DNA, vectors containing same and transformed host cells. Applicants assert that the Mulbry reference does not disclose the sequence, however, the DNA coding for the enzyme is disclosed, and even though not sequenced, that DNA coding for the enzyme inherently has a sequence and that sequence is not changed whether or not that DNA has or has not been subjected to DNA sequencing. The assertion of difficulty in obtaining the sequence is simply not substantiated by factual evidence.

Claims 1-7, 9, 10, 12-13, 30-32, and 37-39 remain rejected and new claim 71 is rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over McDaniel (AZ) for the reasons of record in the prior Office Action.

The comments in the response filed 28 October 1991 have been noted but are not convincing. Applicants assert that the McDaniel reference does not disclose the sequence, however, the DNA coding for the enzyme is disclosed, and even though not sequenced, that DNA coding for the enzyme inherently has a sequence and that sequence is not changed whether or not that DNA has or has not been subjected to DNA sequencing. The assertion of difficulty in obtaining the sequence is simply not substantiated by factual evidence.

Claims 1-3, 5-7, 10, 12-13, 30-32, and 37-39 remain rejected and new claim 71 is rejected under 35 U.S.C. 102 (b) as anticipated by or, in the alternative, under 35 U.S.C. 103 as obvious over Serdar et al. (BC) for the reasons of record in the prior Office Action.

The comments in the response filed 28 October 1991 have been noted but are not convincing. Applicants assert that the Serdar et al. reference does not disclose the sequence, however, the DNA coding for the enzyme is

disclosed, and even though not sequenced, that DNA coding for the enzyme inherently has a sequence and that sequence is not changed whether or not that DNA has or has not been subjected to DNA sequencing. The assertion of difficulty in obtaining the sequence is simply not substantiated by factual evidence and mere assertion that the four year differential (1985 to 1989) is indicative of difficulty in sequencing is unsubstantiated by factual evidence.

Thus, given the above, it is evident that the claimed invention as defined by the claims was as indicated above, anticipated by the references, and if not anticipated, then obvious.

Claims 1-10, 12-16, 30-33, and 37-40 remain rejected and new claim 71 is rejected under 35 U.S.C. 103 as being unpatentable over Luckow et al. taken with all of Wild et al. (AT), Mulbry et al. (AY), McDaniel (AZ), and Serdar et al. (BC) for the reasons of record in the prior Office Action.

Claim 1-16, 30-33 and 37-40 are rejected under 35 U.S.C. 103 as being unpatentable over Luckow et al. taken with all of Wild et al. (AT), Mulbry et al. (AY), McDaniel (AZ), and Serdar et al. (BC) as applied to claims 1-10, 12-16, 30-33, 37-40, and 71 above, and further in view of Old et al. for the reasons of record in the prior Office Action.

The comments regarding the rejections of the claims under 35 U.S.C. 103 beginning at page 32 of the response filed 28 October 1991 are considered here under the rejections for obviousness and are not convincing with regard to the McDaniel et al. (BY), Harper et al. (BX), Wild et al. (AT), Mulbry et al. (AY), McDaniel AZ), and Serdar (BC) references cited in the above grounds of rejection. At the outset, it is noted that applicant has cited Graham v. John Deere with regard to the scope and content of the prior art, the difference between the art and the invention as claimed, the level of skill in the art, and various secondary considerations.

With regard to the scope and content of the prior art, it is pointed out as above, that all of the references are by others. With regard to the Wild

et al. reference, note that the lack of sequence data does not alter sequence of DNA bases that encode the enzyme. The assertion of difficulties in sequencing of the DNA is in the absence of objective evidence, is only assertion and as such, the reference need not teach means of overcoming such alleged difficulties. It is pointed out that the comments in the response assert several "difficulties" but do not state what those difficulties were or even how such difficulties were overcome by the inventors. The assertions of very low amounts of enzyme available for amino acid sequencing is not convincing as it was clearly evident from the available art that only very small amounts of a protein would have been needed for amino acid sequencing. In this regard, attention is directed to Hunkapiller et al. which indicates that it is possible to analyze the sequence of proteins (and enzymes, which are proteins) with as little as 5 and 50 pmol of protein. Thus, absent objective evidence, applicants response is not convincing. The recited pages 9 and 23 of the specification do not indicate that the amount of available enzyme was less than that indicted in the Hunkapiller et al. reference and in any event, the amount needed for sequencing is not a function of the enzymatic activity. With regard to the Wild et al. reference, it is readily apparent that the reference discloses that DNA coding for the enzyme, the issue that Wild et al. does not teach an open reading frame is not convincing as Wild et al. disclose the plasmid(s) containing the DNA coding for the enzyme where such plasmids inherently must contain such open reading frame else the enzyme would not have been expressed. With regard to the issue of the 250 bases, while the reference indicates that removal of 250 base pairs enhanced activity, note that the reference discloses the DNA coding for the enzyme, vectors containing same and transformed host cells. In any event, the Wild et al. reference does not as asserted in the response indicate "the confused state of the art prior to the present invention". Where is this found in the reference?

The citation of Amgen v. Chugai Pharmaceutical Co. Ltd. is noted. It is assumed that the proper cross reference is to 18 USPQ2d 1016. Note that the issue here is not 35 U.S.C. 102 (g) but 35 U.S.C. 102 (a) and/or 35 U.S.C. 103 where the cited references are by others and the relevant date is prior to the

date of invention as determined by the filing date of the present invention. Applicant asserts that the DNA sequence was unknown prior to applicants disclosure in the application, however, such is not the case here as at least one of the references disclose the sequence and where not explicitly set forth, applicant has not shown objective factual evidence to the contrary that the DNA disclosed in the references is different in biological function or that the DNA sequence encoded a different enzyme. Of note is the acquiescence in the response as noted above to alter the DNA sequence shown in Figure 1 of the present specification.

With regard to the Mulbry et al. reference (see the comments starting at page 37), that reference discloses cloning and expression of organophosphate degrading genes from P. diminuta and a Flavobacterium (ATCC 27551) and points out (page 929) that "it was possible to use a cloned DNA fragment that contained the opd gene isolated from an American strain of P. diminuta to recognize the homologous DNA sequence from a Flavobacterium sp isolated in the Philippines. It is pointed out that while the sequence is not disclosed, in the alternative, only routine sequencing of the DNA would have been needed to determine the sequence. Note that applicant has not shown objective factual evidence to the contrary that the DNA disclosed in the reference is different in biological function or that the DNA sequence encoded a different enzyme. Of note is the acquiescence in the response as noted above to alter the DNA sequence shown in Figure 1 of the present specification. The comments assert that Mulbry et al. teaches away from the invention, however, note also the abstract which indicates "... The intact gene (opd, organophosphate-degrading gene) from this degradative plasmid was cloned into M13mp10 and found to express parathion hydrolase under control of the lac promoter ...". Note the disclosure to isolate the same gene from P. diminuta. In any event, applicant also asserts that the reference teaches away from the invention, however, in this situation, following the teachings in the disclosure, the gene, the vector(s) and host cells would have been obtained. In this regard, there is an expected degree of success as the reference indicates positively that the requisite gene was obtained. Attention is directed to In re O'Farrell 7 USPQ2d 1673 (Fed. Cir. 1988) which is one of

many citations indicating obviousness does not require absolute predictability, but only a reasonable expectation of success which from the successful example presented in the reference is a reasonable expectation of success and even where other references would apparently conflict as asserted in the response, those references also present clear examples of success in obtaining the opd gene. Here, attention is directed to In re Young, 18 USPQ2d 1089 (CAFC 1991) at 1091 which indicates as here, that where there are apparently conflicting references, when considered by one of ordinary skill in the art, the suggestive power of the references must be weighed as to the degree to which each reference might accurately discredit another. Here, in each reference, there is a presentation of a successful example, and that given such successful examples, it is apparent that the disclosure of each reference would have permitted the successful isolation of the DNA coding for the opd gene.

With regard to the McDaniel (AZ) reference, the comments starting at page 39 of the response are not convincing. It is of note that the comments are presented by applicants' representative who in this instance is also author of the reference which is applicants' representative's own doctoral dissertation. Those comments apparently assert that the McDaniel (AZ) reference contains serious errors? Note however, that the reference itself indicates the same vectors containing the opd gene and host cells containing the vector. The comments assert that the actual start site was not known, however, as pointed out in the response, the reference page 98, points out that there were two potential start sites, and given such information, it would have been anticipated that one of the two was the actual start site and if not anticipated, it would have been obvious that one of the two was the start site. Thus, the comments are not convincing. The comment regarding the lack of explicit disclosure of the molecular weight of the enzyme is not convincing as the claims are drawn to the DNA, vectors, host cells, and process of producing the enzyme, not the enzyme per se.

With regard to Serdar et al. (BC), the comments in the response starting at page 41 are not convincing. Applicants assert that the Serdar et al.

reference does not disclose the sequence, however, the DNA coding for the enzyme is disclosed, and even though not sequenced, that DNA coding for the enzyme inherently has a sequence and that sequence is not changed whether or not that DNA has or has not been subjected to DNA sequencing. The assertion of difficulty in obtaining the sequence is simply not substantiated by factual evidence and mere assertion that the four year differential (1985 to 1989) is indicative of difficulty in sequencing is unsubstantiated by factual evidence. The issue of down sizing the DNA disclosed in the Serdar et al. reference is not convincing as what that downsizing shows is that the DNA which has been removed is not required to code for amino acid residues necessary for biological activity of the encoded enzyme. Moreover, the comments regarding increased expression are not convincing as the comments at page 42, admit that the high level expression of OPA enzyme was apparently present in the native strains in which the enzyme was first detected.

The response further indicates a "DAN" coding sequence? For the purpose of this Office Action, it is taken that "DAN" refers to "DNA". It is noted that the response indicates that claim 1 refers to an isolated and substantially purified opd gene, however, note the use of "comprising" in the claim, where that use permits the inclusion of any other DNA attached to the 5' and the 3' ends of the DNA coding for the OPD enzyme. Note that isolating the plasmid in this instance is also meets all of the claim requirements where as pointed out the sequence information is inherent to the DNA polymer. Whether or not the DNA polymer coding for the OPD enzyme has been subjected to sequence determination does not alter the sequence of bases coding for the enzyme. Thus, it is not seen that there is a difference between the cited art and the invention defined by claim 1 and even where the comments in the response assert a difference, that difference of the explicit disclosure of the sequence of bases would have been obvious and in any event it is not clear which sequence is the correct sequence especially in view of the acquiescence to alter the sequence shown in Figure 1 of the present application. Note that in claims 6 and 12, absent qualifying terminology, the vector and cell containing the vector are also the same as the naturally occurring plasmid and cell containing that plasmid, thus, claims 6 and 12 do not distinguish over

the cited art. Claim 14, is noted as citing the application of eukaryotic cell, however, the use of a eukaryotic cell as a host cell is well known. Attention is directed to the Luckow et al. and Old et al. references which are both of record.

With regard to the level of ordinary skill in the art (response, starting at page 45) it is noted that the decisions in Standard Oil Co. v. American Cyanamid Co., Ex parte Chicago Rawhide Manufacturing Co., and In re Corkhill have been cited. While it is noted that the Standard Oil Co. v. American Cyanamid Co. decision indicates that one of ordinary skill in the art is not one who innovates, it is not necesary to innovate to take a disclosed plasmid containing a given gene and to place that DNA into other plasmids and host cells as that technique has been used since at least the inception of genetic engineering technology. Moreover, and more recently, In re Nilssen, 7 USPQ2d 1500 (CAFC 1988), indicates that the hypothetical person of ordinary skill in the art is assumed to have knowledge of all prior art in the field of the inventor's endeavor, of prior art solutions for a common problem even if outside the field, and that for the purposes of combining references, those references need not explicitly suggest combining teachings, moreover, note the Kelly reference (page 24, right column) which is one of many indicating the level of ordinary skill in the art. With regard to the motivation to combine (Ex parte Chicago Rawhide Manufacturing Co.), note the Nilssen decision and the fact that all of the cited references are drawn to the same field of endeavor as defined by the claims in the present application. In any event as previously indicated, in the rejection of claims under 35 U.S.C. 103, Luckow et al. disclose that foreign genes are readily expressed using baculoviral vectors and are widely accepted for expression of proteins of agricultural and medical importance (see at least the abstract and the use of S. frugiperda cells, section on EXPERIMENTAL PROTOCOLS) such that one of ordinary skill in the art would have been motivated to use the baculoviral vectors and hosts because the heterologous products produced are biologically active and produce recombinant products very similar to the authentic proteins (page 51) and because the vectors allow "expression of prokaryotic" (here the organophosphorous acid anhydrase DNA, an agriculturally important protein

since it catalyzes the transformation of various organophosphorous pesticides) "or eukaryotic genes to produce fused or non-fused recombinant proteins" for the same advantage of "abundant expression of recombinant proteins" (see page 47). Thus, given what was known in the art, one of ordinary skill in the art would have found it obvious to combine the references with known art recognized techniques to have arrived at the invention, see In re Donohue, 226 USPQ 619 (CAFC 1985) which at page 621, like here, possession of the invention is effected when one of ordinary skill in the art (at least a PhD with some postdoctoral experience) combines the references disclosing the DNA coding for the OPD enzyme on a given plasmid, and which DNA has been cloned by insertion into alternative vectors where absent factual evidence to the contrary, any other alternative vector and host cell would have been an equivalent substitute within the purview of one of ordinary skill in the art. Here, as indicated in the Donohue decision, that description in the art would have sufficed to permit one of ordinary skill in the art to have combined the publications' written description with the ordinary skilled artisans' own knowledge to so as to have arrived at the claimed invention especially where at least Luckow et al. and Old et al. disclose what one of ordinary skill in the art knew and routinely used. Thus, applicants' specification has not been used, implied or needed to reject the claims and the Ex parte Chicago Rawhide Manufacturing Co. decision is distinguished and no use of hindsight is implied, used, intended, or applied. Note that the application of the requisite art to reject the claims is not hindsight and such allegations are not well taken.

The discussion of secondary considerations (starting at page 46 of the response filed 28 October 1991) has been considered but is not convincing. The remarks regarding long felt but unresolved need and the attached exhibits are noted, however, the comments are not commensurate in scope to the invention as claimed. Note that the invention is drawn to the DNA, vectors, host cells, and process of producing an OPD enzyme whereas the comments and exhibits do neither establish a long felt need for the DNA, the vectors, and host cells, nor a process utilizing recombinant DNA technology to produce the enzyme. Note that organophosphorous pesticide sensitivity by certain humans

does not establish such need especially where there is not even an establishment of human use of the recombinant enzyme to ameliorate the effects of organophosphorous pesticides. See the cited exhibits C-I which only establish that various pesticides are toxic to certain livestock and humans at given dosages. This does not establish any long felt need. Note that Exhibit K establishes a method of use of the enzyme, not a need for the DNA, the vectors, host cells, or a process utilizing recombinant DNA technology to produce the enzyme. In Exhibit L, the fact that the U.S. Army has a stockpile of the pesticide and has defined a route of eliminating the pesticide by burning same does not establish a need for the DNA, the vectors, host cells, or a process utilizing recombinant DNA technology to produce the enzyme.

With regard to commercial success, Exhibit M is noted but no facts are presented as to what is part of the development phase and what was to be done. This does not translate into a showing of commercial success especially where as admitted in the response, applicants have no data showing that the DNA, the vector, host cells, and process of culturing same were effective in any commercial endeavor. Since the comments regarding Serdar are not substantiated by presentation of factual evidence in the appropriate declaration format from Serdar, such assertions are not convincing. The response asserts at page 50 that it is "only by copying the methods of the present invention that others were able to produce the sized-down fragment". Note that it is not clear what "others" are referred to and in any event, down-sizing the fragment is not of import as the larger fragment still contains all of the information in the DNA sequence that is in the smaller fragment.

The comments in the response at page 50 assert copying by others, however, it is not clear what is meant as Serdar et al. (BC) and Mulbry et al. (AY) are references which bear publication dates prior to the filing date of the present application. It is not seen how Serdar et al. and Mulbry et al. copied from applicants when the cited references were disclosed prior to applicants' filing date. Thus, the Specialty Composites v. Cabot Corp. decision is distinguished.

Applicants' response at page 51 also asserts the failure of others, however, that is not apparent from the successful examples presented in the cited prior art and in any event, the response does not establish a competitive commercial market, impressive commercial success, the praise of independent commentators, or any performance benefits of the DNA, the vectors, and the host cells. Note that one cannot infringe a nonexistent patent nor do the facts of record presented in the response establish same, thus, the S.C. Johnson & Son, Inc. v. Carter-Wallace, Inc. decision cited by in the response is distinguished. Moreover, the OPA enzyme is not the same composition as the DNA which encodes the enzyme, or the vector containing that DNA or the naturally occurring microorganisms containing the naturally occurring plasmid or the transformed microorganisms containing a chimeric plasmid containing that portion of the DNA excised from the naturally occurring plasmid and which DNA effects expression of that DNA coding for the OPA enzyme as the ultimate product, the enzyme, via the intermediate of an mRNA. See especially the above with regard to Figure 1 of the present application.

No claim is allowed.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, THIS ACTION IS MADE FINAL. See MPEP 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 CFR 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Serial Number 07/344,258
Art Unit 1814

Inquiry regarding this communication should be directed to Christopher Low at telephone number (703) 308-0196.

CSFL
CSF Low
13 January 1992

ROBERT A. WAX
SUPERVISORY PATENT EXAMINER
ART UNIT ~~187~~ 1814